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10/549,987	09/19/2005	Jianming Chen	133697-0006	8330

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EXAMINER	
SCHUBERG, LAURA J	

ART UNIT	PAPER NUMBER
1657	

NOTIFICATION DATE	DELIVERY MODE
04/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/549,987	CHEN ET AL.	
	Examiner	Art Unit	
	LAURA SCHUBERG	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6,10 and 16-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,10 and 16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/17/2009 has been entered.

Claims 1, 2, 4-6, 10, 16-18 have been amended and claims 3, 8, 9, and 15 have been canceled. No claims have been newly added.

Claims 1, 2, 4-7, 10-14 and 16-18 are currently pending and have been examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-7, 10-14 and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the concentration range of CoQ10 as 3 (w/v) ~ 40% (w/w). A concentration range must have the same units of measure for each end value of the range in order to define a proper range. That is it must be either w/v or w/w for the

range values, not both as cited by Applicant. For examination purposes, xlaim 1 is interpreted as having any concentration up to 40% (w/w).

In addition, claim 4 recites a concentration range for CoQ10 as 0.1~20% (w/w). While this range includes only one unit as is proper (w/w), since it is dependent upon claim 1, the range must not include values that are not also included in the range of the parent claim in order to be a proper dependent claim. A proper dependent claim shall not conceivably be infringed by anything that would not also infringe the parent claim (MPEP 608.01 (n)).

Because claims 2, 4-7, 10-14 and 16-18 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Appropriate correction is required.

Priority

Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on an application filed in China on 03/20/2003. Applicant has complied with the requirements of 37 CFR 1.63(c), since the oath, declaration or application data sheet does acknowledge the filing of the foreign application.

The current amendment to the specification filed 07/21/2008 has the incorrect date of the Chinese Priority Patent as March 3, 2003. The correct date is March 20, 2003.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.,* 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2, 4-7, 10, 12-14, 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yatvin (US 6,824,790) in view of Keller (US 2002/0039595), Wen-Jian Lan, et al. (Acta Scientarium Naturalium Universitatis Sunyatseni ,Jan. 2004) and Hoppe et al. (US 6,261,575).

Amended claim 1 is drawn to CoQ10- containing preliposomes for preparing cosmetic compositions, which contain spongiamine in liposome structures of the CoQ10-containing preliposomes wherein the preliposomes contain CoQ10 at a concentration of 3 (w/v) ~40% (w/w).

Dependent claims include wherein the preliposomes are a granular, lyophilized solid; concentrations of CoQ10; and additional lipid components.

Amended claim 6 is drawn to a method of preparing the CoQ10-containing preliposomes for preparing cosmetic compositions of claim 1 which comprises: preparing a lipid solution by one of a) melting CoQ10 and spongiamine; and b) dissolving CoQ10 and spongiamine in an organic solvent; and applying the lipid solution to an underlay to produce the CoQ10-containing preliposomes which contain spongiamine.

Dependent claims include the composition of the underlay; wherein the lipid solution is applied to the underlay by one of several methods; wherein the resulting mixture is subject to at least one of several drying methods and the composition of the underlay.

The limitation "for preparing cosmetic compositions" is an intended use limitation and is only given patentable weight in so far as it requires the claimed composition to be in a form suitable for use as a cosmetic.

Yatvin teaches pharmaceutical compositions and methods of making wherein the proliposomal (preliposomal) compositions include an antioxidant (column 7 lines 16-35), a ceramide and cholesterol (column 7 lines 5-10). The presence of the cholesterol

lowers the melting point of the lipid solution so that a lower temperature may be used to melt the antioxidant and lipid (ceramide) (column 10 lines 31-43). The use of lactose in the method is taught as well as dissolving the components with an organic solvent (column 7 lines 58-column 8 line 2 and column 8 lines 49-column 9 line 9). Yatvin teaches that preliposomes (preliposomes) are an alternative to conventional liposomal formulations and solve the stability problems normally associated with conventional liposomes (column 4 lines 45-52). Yatvin also teaches that modifications or alternatives equivalent thereto are within the spirit and scope of the invention (column 13 lines 57-62).

Yatvin does not specifically teach including coenzyme Q10 as the antioxidant or spongiamine as the ceramide. Yatvin does not teach formulating the composition as a cosmetic.

Keller teaches a method of making a preliposome formulation and then dehydrating it. Biologically active materials for the preliposomal formulation include nutritional supplements and antioxidants such as coenzyme Q10 (page 4 claim 5). Ceramides and sphingolipids are taught as suitable as the lipid component (page 2 para 16). Cholesterol is taught as added to the preliposome formulation (page 2 para 16). Liposomal formulations with ceramides are taught to increase bioavailability of an antioxidant which is poorly absorbed orally (page 1 para 10-page 2).

Wen-Jian Lan et al. teach the discovery of two new ceramides named Spongiamine A and Spongiamine B that were isolated from the sponge *Spongia* sp. (abstract and page 3 of translation). Ceramides are taught to be the main structure for

forming sphingolipids and offer advanced activity in anti-tumor, anti-virus, anti-hepatotoxic and immunization uses as well as highly effective for moisturizing (page 2 of translation). The data show that spongiamine are characterized by the classical structure of ceramides (page 4 of translation).

Applicant's disclosure teaches that methods such as a membrane dispersion method or a melt method or an infuse method to obtain CoQ10-containing liposomes which contain the underlay are known in the prior art (page 4 lines 11-14).

Therefore, one of ordinary skill in the art would have been motivated to include CoQ10 in the method and preliposomal composition of Yatvin as an antioxidant because Keller teaches that CoQ10 is a suitable antioxidant to be used in a preliposomal formulation. One of ordinary skill in the art would have had a reasonable expectation of success because Yatvin teaches that preliposomes are ideally suited for lipophilic compounds and have implications for developing formulations that stabilize encapsulated drugs (page 8 para 97).

One of ordinary skill in the art would have been motivated to include the ceramide spongiamine in the method of Yatvin because Wen-Jian Lan et al. teach the discovery of two new ceramides named Spongiamine A and Spongiamine B that were isolated from the sponge *Spongia* sp. (abstract and page 3 of translation) and have numerous benefits (page 2 of translation). One of ordinary skill in the art would have had a reasonable expectation of success because Wen-Jian Lan et al. teach that spongiamine are characterized by the classical structure of ceramides (page 4 of translation); are the main structure for forming sphingolipids; and Keller teaches that

sphingolipids as well as ceramides are also suitable as the lipid component of a preliposome (page 2 para 16).

One of ordinary skill in the art would have been motivated with a reasonable expectation of success of using the methods of membrane dispersion method or a melt method or an infuse method to obtain CoQ10-containing liposomes which contain the underlay since they are known methods in the prior art as disclosed by Applicant.

Hoppe et al. teach a cosmetic formulation of a composition that contains 0.05-1 % CoQ10 and cholesterol (column 4, lines 35-45). The reference also teaches that it is advantageous to add ceramides to the cosmetic formulations (column 5 lines 45-48) and can be encapsulated in liposomes with ceramides as well (column 6 lines 24-28). The concentration of the ubiquinones in the dermatological products (a group of substances which is taught to include coenzyme Q10 (column 3 lines 10-21)) may also be between 0.001-10% by weight (column 4 lines 35-38). In addition the active substances (which includes coenzyme Q10) can be present in the topical formulations in amounts from 0.001 to 99% by weight (column 4 lines 50-56).

Therefore, one of ordinary skill in the art would have been motivated to incorporate the preliposomal formulations of Yatvin containing CoQ10 and ceramides into cosmetic formulations because Hoppe et al. teach that these ingredients are advantageous for cosmetic skin care products. Additional motivation is provided by the fact that Yatvin teaches that proliposomes are an alternative to liposomes and have numerous advantages regarding stability compared to liposomes. One of ordinary skill in the art would have been motivated to add spongiamine as the ceramide because

Wen-Jian Lan et al. teach that ceramides such as spongiamine are highly effective for moisturizing (page 2 of translation). The concentration of the coenzyme Q10 in the cosmetic composition would have been a matter or routine optimization and experimentation, the artisan of ordinary skill recognizing that the anti-aging properties of the composition would be result effective variables. One of ordinary skill in the art would have had a reasonable expectation of success because Keller teaches that compositions containing CoQ10 in liposomal format can be administered topically as well as orally (page 2 para 15).

Therefore, the combined teachings of Yatvin, Keller, Wen-Jian Lan, et al., and Hoppe et al. render obvious Applicant's invention as claimed.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yatvin (US 6,824,790) in view of Keller (US 2002/0039595), Wen-Jian Lan, et al. (Acta Scientarium Naturalium Universitatis Sunyatseni ,Jan. 2004) and Hoppe et al. (US

6,261,575) as applied to claims 1, 2, 4-7, 10, 12-14, 16-18 above, and further in view of Chen et al. (Journal of Pharmaceutical Sciences, 1987) and Weithmann et al. (US 5,318,987).

Claim 11 is drawn to the method of claim 6 wherein the lipid solution is applied to the underlay using a fluidized bed and the organic solvent is evaporated in the fluidized bed.

The combined teachings of Yatvin, Keller, Wen-Jian Lan, et al. and Hoppe et al render obvious claim 6 as described above, but do not specifically mention using a fluidized bed.

Chen et al. teach that use of a fluidized bed is advantageous for formulating proliposomes because 1) the film coating technology using the fluidized bed is well established and processable; 2) various cores and coating materials are available or easy to prepare; and 3) it is cost effective to prepare liposomes for drug delivery by oral and/or many other routes of administration (page 1, last paragraph).

Weissman et al. teach a method of preparing antioxidant/lipid solutions in a liposomal formulation using a fluidized bed to form tablets that contain carriers such as various sugars (lactose) (column 11-column 12). Weissman et al. also teach that better results are obtained if the lipophilic antioxidants are additionally incorporated during the preparation of liposomes as components thereof (column 51 lines 44-46). These formulations can be used in pharmaceuticals as well as cosmetics (column 9 lines 34-40).

Therefore, one of ordinary skill in the art would have been motivated to use the fluidized bed technology in the method of Yatvin to form the preliposomal composition because of the advantageous taught by Chen et al. above. One of ordinary skill in the art would have had a reasonable expectation of success because Weissman et al. teach that fluidized bed technology has been successfully used to form liposomal formulations with lipophilic antioxidants and CoQ10 is a lipophilic antioxidant.

Therefore, the combined teachings of Yatvin, Keller, Wen-Jian Lan, et al., Hoppe et al, Chen et al. and Weithmann et al. render obvious Applicant's invention as claimed.

Response to Arguments

Applicant's arguments filed 02/17/2009 have been fully considered but they are not persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicant argues that none of the prior art references of record suggests a preliposome that is used in a cosmetic composition that contains CoQ10 at such a high concentration as 3 (w/v) to 40% (w/w), which Applicant's have discovered greatly improves the effect of percutaneous adsorption of CoQ10 in cosmetic formulations. Applicant asserts that Example 4 of Applicant's disclosure demonstrates that CoQ10 improves the stability of preliposomes. Applicant asserts that the teachings of the prior

art of record, properly considered in their entirety, do not lead to, suggest or render obvious Applicant's claimed invention.

This is not found persuasive because Hoppe et al teach that ubiquinones (which include coenzyme Q10) have been used for a long time in cosmetic formulations as antioxidants for protection of oxidation-sensitive substances against decay induced by oxygen free radicals (column 3 lines 10-21). Clearly coenzyme Q10 is expected to improve the stability of a composition. In addition, Hoppe et al teach that the concentrations of ubiquinones in topical formulations are taught to be between 0.001 and 99% by weight. While Hoppe et al does indicate lower concentrations of Co Q10 as preferable, clearly higher concentrations of CoQ10 are also considered suitable.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is

the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (MPEP 2144.05).

In addition, the concentration range cited in claim 1 of 3 (**w/v**) to 40 (**w/w**) % is deemed to be indefinite as a concentration range must be consistent with regard to units of measure (either w/v or w/w, not both) as addressed above in the rejection under 112 2nd.

In submitting evidence asserted to establish unobvious results, there is a burden on an applicant to indicate how the examples asserted to represent the claimed invention are considered to relate to the examples intended to represent the prior art and, particularly, to indicate how those latter examples do represent the closest prior art. See *In re Borkowski*, 595 F.2d 713, 184 USPQ 29 (CCPA 1974); *In re Goodman*, 339 F.2d 228, 144 USPQ 30 (CCPA 1964).

The evidence relied upon should also be reasonably commensurate in scope with the subject matter claimed and illustrate the claimed subject matter "as a class" relative to the prior art subject matter "as a class." *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971); *In re Hostettler*, 429 F.2d 464, 166 USPQ 558 (CCPA 1970). See, also, *In re Lindner*, 457 F.2d 506, 173 USPQ 356 (CCPA 1972).

It should also be established that the differences in the results are in fact unexpected and unobvious and of both statistical and practical significance. *In re Merck*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); *In re Longi*, 759 F. 2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Klosak*, 455 F2d 1077, 173 UAPQ 14 (CCPA 1972); *In*

re D'Ancicco, 429 F.2d 1244, 169 USPQ 303 (CCPA 1971). *Ex parte Gelles*, 22 USPQ2d 1318 (BPAI 1992).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA SCHUBERG whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Laura Schuberg